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Original Article

Body composition in the elderly: Reference values and bioelectrical impedance spectroscopy to predict total body skeletal muscle mass☆

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SUMMARY

Background & aims: To validate the bioelectrical impedance spectroscopy (BIS) model against dual-energy X-ray absorptiometry (DXA), to develop and compare BIS estimates of skeletal muscle mass (SMM) to other prediction equations, and to report BIS reference values of body composition in a population-based sample of 75-year-old Swedes.

Methods: Body composition was measured by BIS in 574 subjects, and by DXA and BIS in a subset of 98 subjects. Data from the latter group was used to develop BIS prediction equations for total body skeletal muscle mass (TBSMM).

Results: Average fat free mass (FFM) measured by DXA and BIS was comparable. FFM_{BIS} for women and men was 40.6 kg and 55.8 kg, respectively. Average fat free mass index (FFMI) and body fat index (BFI) for women were 15.6 and 11.0. Average FFMI and BFI for men were 18.3 and 8.6. Existing bioelectrical impedance analysis equations to predict SMM were not valid in this cohort. A TBSMM prediction equation developed from this sample had an R^2_{pred} of 0.91, indicating that the equation would explain 91% of the variability in future observations.

Conclusions: BIS correctly estimated average FFM in healthy elderly Swedes. For prediction of TBSMM, a population specific equation was required.

1. Introduction

Bioelectrical impedance analysis (BIA) is an easily performed and non-invasive way to measure body composition.[1–3] Single frequency-BIA (SF-BIA) is commonly used to calculate total body water (TBW) and fat free mass (FFM).[2] Multi frequency-BIA (MF-BIA)[2] and bioelectrical impedance spectroscopy (BIS) calculate intracellular water (ICW), extracellular water (ECW), TBW and FFM. Thus, BIS offers information of ICW and ECW distribution, and FFM is predicted from these. Body fat (BF) is generally calculated as the difference between body weight (BW) and FFM.

There is an increasing interest to specifically estimate skeletal muscle mass (SMM), as it may better reflect the body protein reserves and nutritional status in disease and aging.[4] SMM loss (sarcopenia) is a process associated with aging as well as with several diseases.[4] In healthy elderly, development of sarcopenia may be masked by weight stability.[5] Furthermore, aging is associated with decreased TBW, bone mass, body cell mass (BCM) and FFM.[1] Hence, due to the age dependent changes in body composition, it would be useful to obtain BIS reference values for the elderly.

BIS-measured segmental total water volume has previously been reported to be larger than, but highly correlated with, segmental muscle volume measured by magnetic resonance imaging (MRI), and BIS also tracked changes associated with head-down tilt.[6] Furthermore, BIS successfully predicted total body skeletal muscle mass (TBSMM) in a cohort with hemodialysis patients.[7]

There are several published prediction equations to estimate SMM by BIA. A SF-BIA equation was suggested to predict whole body SMM ($SMM_{Janssen}$) among healthy Caucasians aged 18–86 years, validated against MRI.[8] Another SF-BIA equation used data from healthy volunteers aged 22–94 years, to predict appendicular skeletal muscle mass ($ASMM_{Kyle}$), validated against appendicular lean soft tissue (ALST) measured by dual-energy X-ray absorptiometry (DXA) ($ALST_{DXA}$).[4] However, the use of general BIA

Abbreviations: BIS, bioelectrical impedance spectroscopy; BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; SMM, skeletal muscle mass; TBSMM, total body skeletal muscle mass; FFM, fat free mass; BF, body fat; fatness, percentage body fat; FFMI, fat free mass index; BFI, body fat index; SMMI, skeletal muscle mass index.

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prediction equations across different ages and ethnic groups without prior testing of their validity should be avoided.[2] Thus, it was reported that $ASMM_{Kyle}$ was invalid in patients with chronic kidney disease.[9]

DXA is increasingly accepted as reference method to evaluate BIS.[2] DXA yields information on BF, lean soft tissue (LST) and bone mineral content (BMC). The extremities consist primarily of three components: skeleton, fat and SMM, and limb LST has been shown to represent ASMM.[10] Furthermore, DXA has been validated against MRI to predict TBSMM ($TBSMM_{DxA}$).[11]

The aims of this study were to validate BIS against DXA and to report BIS reference values of body composition among elderly Swedes for use in evaluation of body composition changes in disease and aging. Furthermore, we wanted to investigate the validity of existing BIA-equations to predict SMM in our population, and if needed, to develop a regression equation for the prediction of TBSMM from BIS. Finally, we wanted to evaluate the extent to which BIS measurements were accurate compared to previously reported SF-BIA predictors.[4,8]

2. Materials and methods

2.1. Subjects

The subjects were participants in the Geriatric and Gerontologic Population Study and the Population Study of Women in Göteborg, Sweden. The study was a follow-up of a population-based survey of 70-year olds that had been recruited 5 years previously and the protocol was approved by the regional ethics committee in Göteborg. 1332 subjects (788 women and 544 men) were selected based on date of birth during the year 1930, in order to be representative of their birth cohort living in that area. 839 (501 women and 338 men) participated, which corresponds to a participant frequency of 63% (64% women and 62% men).

597 non-institutionalized 75-year-old subjects were included in the survey described here, and all were examined by BIS. Measurements from 23 subjects were excluded due to technical problems or biologically implausible data (not excellent model fit (11), Fc < 20 Hz (3) or >100 Hz (6), Ri < Re (1), FFM_{BIS} > 95% of BW (1), ECW/ICW-ratio < 0,54 (1)). Thus, 345 women and 229 men were included. Information of medication use is presented in Table 1. 107 subjects of 574 had no medication. 81 women (24%) and 26 men (11%) used diuretics. A subset of 120 subjects was examined by DXA and BIS, but 22 were excluded due to presence of methal protheses. Thus, 48 women and 50 men were included. All 98 fullfilled the same BIS inclusion criteria as above. For the 98 subjects examined by DXA and BIS, there was information on medication use available for 87 subjects. 14 (16%) used diuretics. Distribution of BMI for both groups is presented in Table 2.

Table 1
Medication. Percentage of medication use in 574 non-institutionalized 75-year-old subjects measured by BIS at Vasa Hospital (V-BIS).

Drugs	Women ($n=345$) %	Men ($n=229$) %
Antidiabetic drugs	7	12
Drugs for heart disease, including nitrates	6	11
Antihypertensive drugs	1	2
Diuretics	24	11
Betareceptor-antagonistic drugs	24	27
Calcium-antagonistic drugs	10	14
Drugs affecting the renin–angiotensin system	17	27
Drugs affecting serum lipid levels	19	21
Sex hormones	15	0
Pituitary- and hypothalamic hormones	1	0
Corticosteroids for systemic use	3	2
Thyroid hormone and antithyroid substances	21	3
Cytostatic and cytotoxic drugs	1	1
Drugs for gout	0	4
Analgetics	29	10
Neuroleptics-, sedatives- and sleeping drugs	17	10
Psychoanaleptic drugs, including SSRI	10	5
Drugs for obstructive airway diseases	9	6

2.2. Study design

574 subjects were examined once by BIS at the H70 clinical examination center, formerly Vasa Hospital (V-BIS), Göteborg, Sweden, to obtain reference values of body composition measured by BIS. The validation subgroup of 98 subjects was examined by BIS (D-BIS) and on the same occasion by DXA at Sahlgrenska University Hospital. 87 of the 98 subjects were also measured by V-BIS, and thus participated in the 574 cohort. The results of the validation-group were compared to the previously reported muscle mass prediction equations $ASMM_{Kyle}$[4] and $SMM_{Janssen}$[8]

1. $ASMM_{Kyle}$: $-4.211 + (0.267 \times \text{height}^2/\text{resistance}) + (0.095 \times \text{weight}) + (1.909 \times \text{sex}(\text{men}=1, \quad \text{women}=0)) + (-0.012 \times \text{age}) + (0.058 \times \text{reactance})$
2. $SMM_{Janssen}$: $(\text{height}^2/\text{resistance} \times 0.401) + (\text{gender}(\text{men}=1, \text{women}=0) \times 3.825) + (\text{age} \times -0.071) + 5.102$

Furthermore, data from the validation-group was used to develop and evaluate BIS prediction equations of TBSMM. Three TBSMM-equations with different independent variables were developed by stepwise multiple regression with $TBSMM_{DxA}$ as dependent variable. First, a SF-BIA equation: $TBSMM_{50\ kHz}$ (gender, height in cm (Ht), BW, R(resistance)$_{50\ kHz}$ and Xc(reactance)$_{50\ kHz}$ included). Second, an equation using BIS model predictors: $TBSMM_{BW}$ (gender, Ht, BW, C_m, Re and Ri included). Finally, a BIS equation without BW as predictor: $TBSMM_{noBW}$ (gender, Ht, C_m, Re and Ri included). The predictive value of the equations was evaluated using PRESS statistics (predictive residual sum of squares), see Section 2.5.

2.3. Bioelectrical impedance spectroscopy

Bioimpedance analysis was carried out using Xitron Hydra 4200 devices (Xitron Technologies, San Diego, USA) at both V-BIS and D-BIS. The subjects rested in supine position for 5 min before the tetrapolar whole body measurement with electrodes on the dorsal surface of the right hand/wrist and at the right foot/ankle according to the manufacturer's instructions.[12] Red Dot™ surveillance electrode (2239) for single use with foam tape and sticky gel Ag/AgCl (3M™, Sollentuna, Sweden) was used at both V-BIS and D-BIS. Software Boot version 1.02 and Main version 1.42 were used. ECW and ICW were calculated from Xitron equations[12,13]:

$$ECW = \left[\rho_{ECW} * K_B * \text{Ht}^2 * (\text{BW}/D)^{0.5}/R_0\right]^{(2/3)} \quad (1)$$

where ρ_{ECW} is extracellular resistivity (women: 39 Ω cm, men:

Table 2
BMI. Distribution of BMI among 574 non-institutionalized 75-year-old subjects measured by BIS at Vasa Hospital (V-BIS) and of 98 non-institutionalized 75-year-old subjects measured by BIS at Sahlgrenska University Hospital (D-BIS).

BMI	Women V-BIS ($n=345$) %	Men V-BIS ($n=229$) %	Women D-BIS ($n=48$) %	Men D-BIS ($n=50$) %
<16	0	0	0	0
<18.5	1.2	0	4.2	0
>25	61.4	68.6	60.4	70.0
>30	20.3	16.2	27.1	14.0
>34	5.2	3.1	8.3	0

Table 3
Body composition by BIS. Anthropometrical data and body composition estimates of a population-based sample of 574 75-year-old subjects measured by BIS at Vasa Hospital (V-BIS) and of a validation subgroup of 98 non-institutionalized 75-year-old subjects measured by BIS at Sahlgrenska University Hospital (D-BIS). $FFMI_{BIS}$ = fat free mass index. $SMMI_{BIS}$ = skeletal muscle mass index, calculated as $TBSMM_{noBW}$/(height in m^2). BFI_{BIS} = body fat index. Mean (SD) and percentiles.

	Women (n = 345)	V-BIS	Population sample	Men (n = 229)	V-BIS	Population sample	Women (n = 48)	D-BIS	Validation subgroup	Men (n = 50)	D-BIS	Validation subgroup
	Mean (SD)	Perc. 5	Perc. 95	Mean (SD)	Perc. 5	Perc. 95	Mean (SD)	Perc. 5	Perc. 95	Mean (SD)	Perc.5	Perc. 95
Height (cm)	161 (6.1)	151	171	175 (6.4)	164	185	162 (6.6)	149	173	175 (6.6)	165	189
Weight (kg)	69.2 (12.2)	51.4	90.7	82.1 (12.7)	61.8	106.6	70.9 (14.1)	52.3	97.5	82.0 (11.4)	62.2	102.5
BMI (kg/m^2)	26.5 (4.5)	20.3	34.6	26.9 (3.7)	21.5	33.2	27.0 (5.0)	18.8	36.3	26.6 (3.0)	20.7	32.3
FFM_{BIS} (kg)	40.6 (6.1)	31.1	50.9	55.8 (8.5)	42.9	71.3	41.7 (7.2)	31.8	55.5	57.7 (9.4)	41.5	74.4
BF_{BIS} (kg)	28.6 (8.5)	15.7	43.5	26.3 (8.5)	14.0	39.2	29.2 (8.8)	17.1	45.7	24.3 (6.3)	14.0	35.8
$FFMI_{BIS}$ (kg/m^2)	15.6 (2.2)	12.1	19.5	18.3 (2.5)	4.2	22.9	15.9 (2.5)	11.9	21.0	18.7 (2.4)	14.2	23.0
$Fatness_{BIS}$ (%)	40.7 (6.8)	28.4	50.7	31.7 (7.3)	19.5	43.6	40.6 (5.9)	30.9	50.2	29.6 (6.4)	20.4	40.7
BFI_{BIS} (kg/m^2)	11.0 (3.2)	6.1	16.4	8.6 (2.7)	4.7	12.4	11.1 (3.2)	6.1	16.9	7.9 (2.1)	4.6	10.9
$TBSMM_{noBW}$ (kg)	17.4 (2.9)	12.4	21.7	26.3 (3.0)	20.8	31.0	18.1 (3.2)	13.2	23.9	27.2 (3.4)	21.8	33.2
$SMMI_{BIS}$ (kg/m^2)	6.6 (0.9)	5.1	7.9	8.6 (0.7)	7.5	9.6	6.9 (0.9)	5.5	8.3	8.8 (0.6)	7.5	9.6
Re (ohm)	679 (73)	564	803	574 (73)	459	701	638 (70)	532	766	539 (63)	430	648
Ri (ohm)	1600 (289)	1160	2147	1308 (242)	935	1750	1581 (284)	1122	2073	1261 (231)	959	1811
Phase angle	5.19 (0.62)	4.23	6.23	5.54 (0.62)	4.45	6.66	5.06 (0.63)	4.22	6.39	5.49 (0.60)	4.54	6.58
ECW (l)	14.1 (1.8)	11.2	16.9	19.1 (2.6)	14.6	24.2	14.8 (2.2)	11.5	19.5	20.0 (2.8)	15.6	25.3
ICW (l)	16.5 (3.0)	12.0	21.4	22.8 (4.0)	16.9	29.9	16.7 (3.4)	11.8	23.6	23.4 (4.3)	16.0	31.0
ECW/ICW	0.87 (0.10)	0.69	1.05	0.84 (0.09)	0.69	1.01	0.90 (0.10)	0.71	1.08	0.86 (0.08)	0.73	1.02

40.5 Ω cm), Ht is body height (cm), BW is body weight (kg), D is body density (1.05 kg/l) and $K_B = 4.3$ is a shape factor.[12]

$$ICW = ECW*\left[\left(\left(\rho_{TBW}*R_0\right)/\left(\rho_{ECW}*R_{inf}\right)\right)^{(2/3)}-1\right] \quad (2)$$

where total body resistivity ρ_{TBW} was calculated as

$$\rho_{TBW} = \rho_{ICW} - \left(\rho_{ICW} - \rho_{ECW}\right) \times \left(R_{inf}/R_0\right)^{(2/3)} \quad (3)$$

and ρ_{ICW} is intracellular resistivity (women: 264.9 Ω cm, men: 273.9 Ω cm).

The equation used by the BIS proprietary software to predict FFM_{BIS} is:

$$FFM_{BIS} = \left(\delta_{ECW}*ECW\right) + \left(\delta_{ICW}*ICW\right) \quad (4)$$

where δ_{ECW} is 1.106 kg/l and δ_{ICW} is 1.521 kg/l.[12] BF_{BIS} was calculated as BW minus FFM_{BIS}. In order to compare with previously published BIA-equations,[4,8] 50 kHz-resistance and -reactance values were calculated from the Cole–Cole model parameters obtained from BIS, using Matlab (Matlab®, R2006b, Mathworks). In order to compare body composition to a previous birth cohort, FFM and fatness (percentage body fat) were also calculated according to the BIA FFM-equation used by Dey et al.[1]

2.4. Dual-energy X-ray absorptiometry

DXA was performed by a Lunar Prodigy scanner (Scanex, Helsingborg, Sweden). Whole body scans were performed and BF_{DxA}, LST and BMC were analysed (software version 8.70.005). FFM_{DxA} was defined as the sum of LST and BMC. $ALST_{DxA}$ was defined as the sum of LST in arms and legs.[11] $TBSMM_{DxA}$ was calculated as ($TBSMM_{DxA} = (1.19 \times ALST_{DxA}) - 1.65$) according to model 1 by Kim et al.[11] The precision of the DXA equipment was estimated from repeated measurements on different days in 9 subjects with coefficients of variation of BMC 1.1%, LST 1.1% and BF_{DxA} 2.4%.

2.5. Statistics

SPSS (SPSS, 14.0 and 16.0 for Windows, SPSS Inc.) was used for all statistical analysis, except PRESS and 50 kHz (resistance and reactance)-values which were calculated in Matlab (Matlab®, R2006b, Mathworks). A p-value ≤ 0.05 was considered significant. The descriptive statistics are presented as mean, standard deviation (SD) and percentiles (5% and 95%). Differences between methods were examined by paired samples t test. Differences between groups were examined by independent samples t test. All t tests were adjusted using Bonferroni correction.[14] The relationship between differences in FFM and TBSMM respectively, measured by DXA and BIS and other variables were examined by scatter-dot graphs and linear regression. Stepwise multiple regression was used to predict TBSMM from BIS, validated against DXA. The developed muscle equations were cross-validated with PRESS statistics. In PRESS, each subject in the total data set is excluded, one at a time, and a regression analysis is performed. The value for each omitted subject is predicted, and the difference from the

Table 4
Body composition in elderly. Comparison of body composition in 5 elderly populations, presented as mean (SD).

	n	Weight (kg)	BMI	FFM (kg)	BF (kg)	Fatness (%)
H75/1930[a]						
Women	345	69.2 (12.2)	26.5 (4.5)	40.6 (6.1)	28.6 (8.5)	40.7 (6.8)
Men	229	82.1 (12.7)	26.9 (3.7)	55.8 (8.5)	26.3 (8.5)	31.7 (7.3)
H75/1930: FFM-Dey[b]						
Women	345	69.2 (12.2)	26.5 (4.5)	43.9 (4.2)	25.2 (9.1)	35.4 (7.2)
Men	229	82.1 (12.7)	26.9 (3.7)	58.6 (6.2)	23.5 (8.7)	27.9 (6.6)
NORA75/1915-16[c]						
Women	138	65.3 (10.3)	25.4 (3.6)	42.5 (4.0)	22.8 (7.2)	34.1 (6.1)
Men	115	77.8 (10.4)	25.7 (3.1)	56.1 (4.7)	21.7 (7.1)	27.3 (6.0)
NHANES III[d]						
Women	538	67.1 (14.5)	26.7 (5.3)	42.3 (6.5)	24.8 (9.3)	35.9 (6.9)
Men	447	79.3 (13.3)	26.7 (4.0)	59.1 (8.6)	20.3 (6.8)	25.1 (5.5)
Geneva[e]						
Women	198	64.8 (10.9)	25.9 (4.2)	41.0 (4.9)	23.7 (7.2)	35.9 (5.7)
Men	148	75.1 (10.4)	25.5 (3.3)	56.3 (5.9)	18.8 (6.0)	24.6 (5.1)
Italy DXA[f]						
Women	267	62.2 (7.9)	25.9 (3.0)	38.6 (4.2)	23.1 (5.5)	36.6 (5.5)
Men	78	77.0 (7.0)	26.8 (2.1)	55.9 (4.3)	20.2 (4.0)	26.0 (3.7)

[a] Body composition measured by BIS in Swedish 75-year olds born 1930.
[b] Body composition measured by BIS in Swedish 75-year olds born 1930; calculated according to the FFM SF-BIA equation used in the Swedish NORA75 cohort.[1]
[c] Body composition measured by BIA in Swedish 75-year olds born 1915–16.[1]
[d] Body composition measured by BIA in American non-Hispanic white 70–80-year olds.[19]
[e] Body composition measured by BIA in Swiss 70–79-year olds, calculated according to Geneva equations.[21]
[f] Body composition measured by DXA in an Italian nationally representative cohort aged 70–80 year.[22]

Table 5
Body composition by DXA. Results of DXA measured in 98 non-institutionalized 75-year-old subjects. $FFMI_{DxA}$ = fat free mass index. BFI_{DxA} = body fat index. $ALST_{DxA}$ = appendicular lean soft tissue. $TBSMM_{DxA}$ = total body skeletal muscle mass, calculated as $1.19 \times ALST_{DxA} - 1.65$.[11] $SMMI_{DxA}$ = skeletal muscle mass index, calculated as $TBSMM_{DxA}$/(height in m^2).

	FFM_{DxA} (kg)	BF_{DxA} (kg)	$Fatness_{DxA}$ (%)	$FFMI_{DxA}$ (kg/m^2)	BFI_{DxA} (kg/m^2)	$ALST_{DxA}$ (kg)	$TBSMM_{DxA}$ (kg)	$SMMI_{DxA}$ (kg/m^2)
Women ($n = 48$)								
Mean (SD)	42.4 (5.2)	28.2 (10.5)	38.8 (8.1)	16.1 (1.3)	10.8 (3.9)	16.8 (2.3)	18.4 (2.7)	7.0 (0.7)
Percentiles 5	34.2	10.4	19.9	14.2	3.6	12.5	13.2	5.7
Percentiles 95	53.1	45.7	49.5	19.2	17.3	21.0	23.3	8.2
Men ($n = 50$)								
Mean (SD)	58.2 (7.9)	23.9 (6.8)	28.8 (6.3)	18.9 (1.7)	7.8 (2.3)	24.4 (3.6)	27.4 (4.3)	8.9 (1.0)
Percentiles 5	46.7	10.8	17.3	15.8	3.6	18.4	20.3	6.8
Percentiles 95	74.6	35.7	40.9	21.9	11.5	30.9	35.2	10.2

observed value is the PRESS residual. The sum of squares of the PRESS residuals yields the PRESS statistic.[15] R^2_{pred} from PRESS gives information about the regression equation's predictive capacity; i.e. R^2_{pred} will explain the expected variability in prediction of new observations.[16] R^2 represents the coefficient of determination for the regression equation among the observed subjects. SSE is the sum of squares of the error for the equation. Furthermore, results calculated from the developed equations were compared to each other with paired samples t test. Systematic differences between $TBSMM_{DxA}$ and BIS regression equations, FFM_{DxA} and FFM_{BIS} and BF_{DxA} and BF_{BIS} were examined by Bland–Altman plots.[17]

3. Results

3.1. Body composition measured by BIS

A summary of average body composition data for the cohort with 574 subjects and the subset with 98 subjects is presented in Table 3. Estimates of body composition calculated according to a previously used BIA FFM prediction equation[1] are presented in Table 4.

3.2. Diuretics

Average BMI was significantly higher among the subjects with use of diuretics (27.8) compared to subjects without diuretics (26.4). There were no significant differences in ECW, ICW or FFM_{BIS} between the groups ($n = 574$).

3.3. Comparing body composition measured by BIS and DXA

Body composition measured by DXA is presented in Table 5. Average FFM_{BIS} did not differ from FFM_{DxA} (Table 6), neither when analysed in subgroups with ($n = 14$, $p = 0.58$) or without ($n = 71$, $p = 0.24$) use of diuretics. Average difference of FFM_{DxA} minus FFM_{BIS} was 0.62 kg for women and 0.56 kg for men. There was a strong significant correlation between FFM_{DxA} and FFM_{BIS}, $R = 0.93$, SEE = 4.4 kg. However, the Bland–Altman plot revealed a slight but statistically significant systematic tendency of BIS to increase FFM bias with increasing FFM values (Fig. 1a). A higher ECW/ICW-ratio ($R = 0.63$), Ri ($R = 0.65$) or a lower BMI ($R = 0.53$) or C_m ($R = 0.61$), increased the underestimation of FFM from BIS. Average BF_{BIS} did not differ from BF_{DxA} (Table 6). Average difference of BF_{DxA} minus BF_{BIS} was −0.97 kg for women and −0.40 kg for men. However, the Bland–Altman plot revealed a significant small systematic negative bias (Fig. 1b), reciprocal to the FFM_{BIS} bias.

3.4. Skeletal muscle mass estimates

$SMM_{Janssen}$ overestimated TBSMM compared to DXA (Table 6). Also, $ASMM_{Kyle}$ overestimated ALST compared to DXA (Table 6).

3.5. BIA and BIS prediction equations of TBSMM

The electrical parameters of the BIS measurements (Re, Ri and C_m) were entered in the model for $TBSMM_{BW}$ and $TBSMM_{noBW}$, but C_m was found not to be significant.

BIA- and BIS-equations:

1. $TBSMM_{50\,kHz} = -24.021 + (0.33 \times Ht) + (-0.031 \times R_{50\,kHz}) + (0.083 \times Xc_{50\,kHz}) + (-1.58 \times gender) + (0.046 \times BW)$
2. $TBSMM_{BW} = -23.953 + (0.333 \times Ht) + (-0.004 \times Ri) + (-0.010 \times Re) + (-1.727 \times gender) + (0.042 \times BW)$
3. $TBSMM_{noBW} = -24.05 + (0.365 \times Ht) + (-0.005 \times Ri) + (-0.012 * Re) + (-1.337 * gender)$

Ht: height in cm. Gender: women = 1, men = 0.

For regression model summary and PRESS statistics, see Table 7. Average differences for the equations compared to $TBSMM_{DxA}$ were 0.17 kg/−0.10 kg/0.22 kg for $TBSMM_{50\,kHz/BW/noBW}$ respectively (Table 8). Bland–Altman plots did not reveal any significant systematic bias for any of the three equations (Fig. 1c-e). When applied to the group with 574 subjects (Table 9), there were small but mostly significant differences between the developed equations. $TBSMM_{noBW}$ and $SMM_{Janssen}$ differed significantly. There were no systematic biases found when differences between $TBSMM_{DxA}$ and $TBSMM_{noBW}$ and single predictors (BMI, Re, Ri, C_m, ECW, ICW, alfa, Td, Fc, ECW/ICW, FMI_{DxA}) were examined by scatter-dot graphs and linear regression.

Table 6
Comparison of BIS and DXA. Differences of FFM and BF measured by DXA and BIS, BIA skeletal muscle mass estimates[4,8] and muscle mass measured by DXA, in 98 non-institutionalized 75-year-old subjects, compared with paired samples t test. $ALST_{DxA}$ = appendicular lean soft tissue. $TBSMM_{DxA}$ = total body skeletal muscle mass, calculated as $1.19 \times ALST_{DxA} - 1.65$.[11] ns = Non-significant.

	Mean (SD)	p-value
Women ($n = 48$)		
FFM_{DxA} minus FFM_{BIS} (kg)	0.62 (4.10)	ns
BF_{DxA} minus BF_{BIS} (kg)	−0.97 (4.12)	ns
$TBSMM_{DxA}$ minus $SMM_{Janssen}$ (kg)	−1.02 (1.39)	<0.03
$ALST_{DxA}$ minus $ASMM_{Kyle}$ (kg)	−0.64 (1.41)	0.01
Men ($n = 50$)		
FFM_{DxA} minus FFM_{BIS} (kg)	0.56 (4.62)	ns
BF_{DxA} minus BF_{BIS} (kg)	−0.40 (4.60)	ns
$TBSMM_{DxA}$ minus $SMM_{Janssen}$ (kg)	−4.05 (2.22)	<0.03
$ALST_{DxA}$ minus $ASMM_{Kyle}$ (kg)	−1.23 (1.63)	<0.03

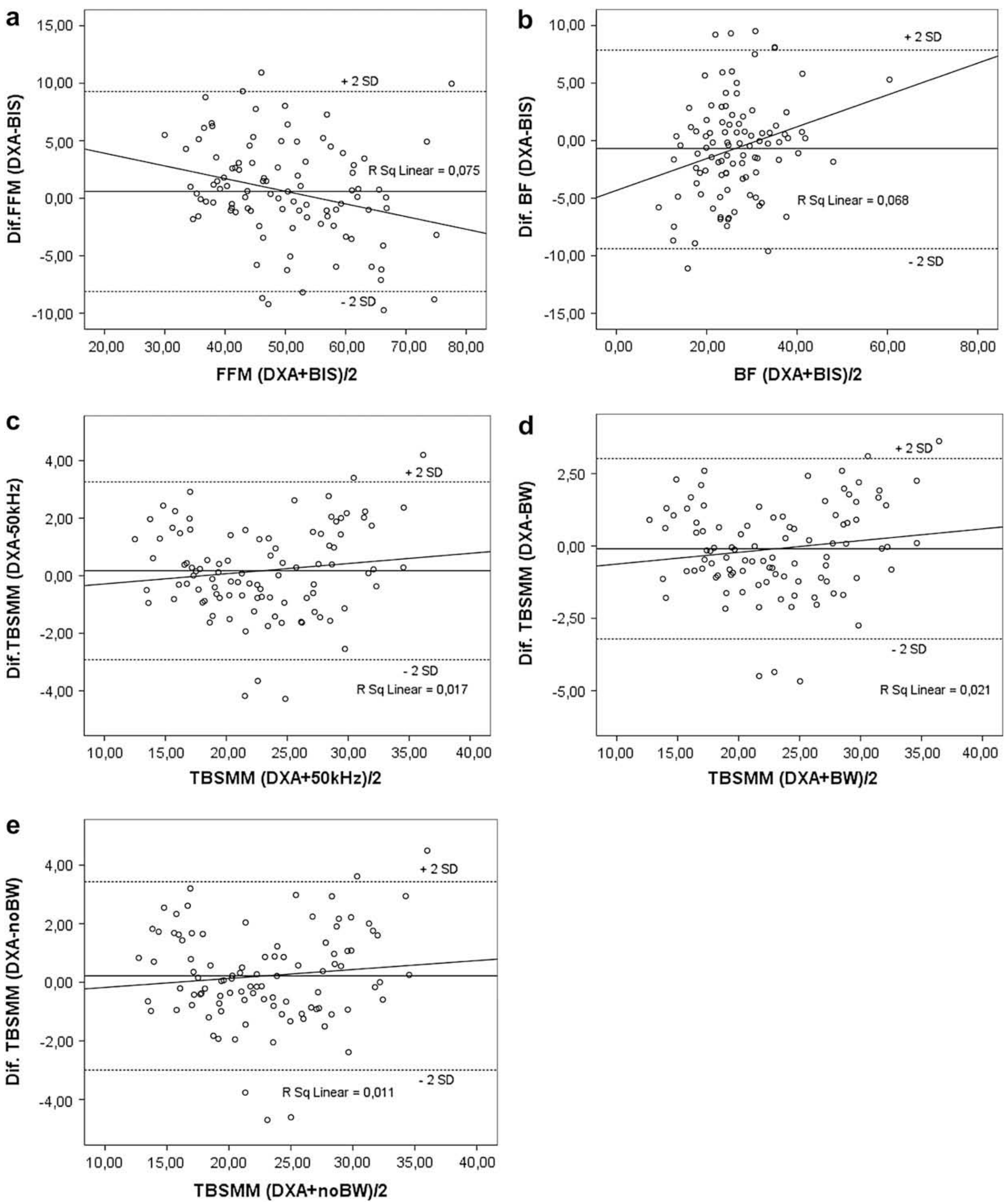

Fig. 1. (a) Bland–Altman plot comparing FFM_{DxA} and FFM_{BIS} in 98 non-institutionalized 75-year-old subjects. Horizontal line = mean difference (kg). Dotted lines = ±2 SD. Regressionline: difference between FFM_{DxA} minus FFM_{BIS} as dependent variable and mean of FFM_{DxA} and FFM_{BIS} as independent variable. Regressionline: $R = 0.27$, $p = 0.007$. (b) Bland–Altman plot comparing BF_{DxA} and BF_{BIS} in 98 non-institutionalized 75-year-old subjects. Horizontal line = mean difference (kg). Dotted lines = ±2 SD. Regressionline: difference between BF_{DxA} minus BF_{BIS} as dependent variable and mean of BF_{DxA} and BF_{BIS} as independent variable. Regressionline: $R = 0.26$, $p = 0.009$. (c) Bland–Altman plot comparing $TBSMM_{DxA}$ and equation $TBSMM_{50\ kHz}$ in 98 non-institutionalized 75-year-old subjects. Horizontal line = mean difference (kg). Dotted lines = ±2 SD. Regressionline: difference between $TBSMM_{DxA}$ and $TBSMM_{50\ kHz}$ as dependent variable and mean value of $TBSMM_{DxA}$ and $TBSMM_{50\ kHz}$ as independent variable. $R = 0.13$, $p = 0.21$. (d) Bland–Altman plot comparing $TBSMM_{DxA}$ and equation $TBSMM_{BW}$ in 98 non-institutionalized 75-year-old subjects. Horizontal line = mean difference (kg). Dotted lines = ±2 SD. Regressionline: difference between $TBSMM_{DxA}$ and $TBSMM_{BW}$ as dependent variable and mean value of $TBSMM_{DxA}$ and $TBSMM_{BW}$ as independent variable. $R = 0.15$, $p = 0.15$. (e) Bland–Altman plot comparing $TBSMM_{DxA}$ and equation $TBSMM_{noBW}$ in 98 non-institutionalized 75-year-old subjects. Horizontal line = mean difference (kg). Dotted lines = ±2 SD. Regressionline: difference between $TBSMM_{DxA}$ and $TBSMM_{noBW}$ as dependent variable and mean value of $TBSMM_{DxA}$ and $TBSMM_{noBW}$ as independent variable. $R = 0.11$, $p = 0.29$.

Table 7
TBSMM prediction equations. Regression model summary and results of PRESS (predictive residual sum of squares) statistics for BIS TBSMM prediction equations, developed by stepwise multiple regression in 98 non-institutionalized 75-year-old subjects.

	R	R^2	SEE (kg)	SSE	PRESS	R^2_{pred}
$TBSMM_{50\ kHz}$	0.96	0.93	1.59	231.4	265.9	0.92
$TBSMM_{BW}$	0.96	0.93	1.60	235.6	270.5	0.92
$TBSMM_{noBW}$	0.96	0.92	1.64	249.6	278.7	0.91

4. Discussion

We found BIS, using Xitron equations, to be valid for estimating average FFM in non-institutionalized elderly Swedes when compared to DXA. However, previously published BIA prediction equations for SMM[4,8] were found not to be valid in this cohort. New BIS muscle mass equations could successfully predict average TBSMM, although with substantial individual variation.

4.1. Study limitations

We included subjects regardless of BMI, although BIA has only been shown to be valid up to BMI 34, according to a recent review.[3] The disproportion between body mass and body conductivity lowers the accuracy of BIA in obesity.[3] FFM in obese subjects might be overestimated by BIA.[18] However, a purpose of this study was to be representative for the elderly population, and hence the 29 obese subjects with BMI > 34 were included. No technical problems were encountered with the DXA examinations among subjects with BMI > 34.

4.2. Body composition in the elderly

We have previously validated SF-BIA against a four-compartment model (4-C model) based on TBK and TBW in a random sample of 75-year-old subjects born 1915–16 from the NORA75 cohort.[1] In the 1915–16 cohort, women had higher average fatness than men, 34% and 27% respectively.[1] The difference in fatness between genders was confirmed in this report, the BIS average values reported here were 41% and 32%, in women and men respectively (Table 4). However, when the current measurements were calculated according to the FFM-equation used in the NORA75 cohort (FFM_{Dey}), average FFM was significantly higher (Table 4). Furthermore, average fatness was more in agreement with the 1915–16 cohort. Thus, non-institutionalized elderly Swedes appear well-nourished, with a trend of increasing BW and BMI.

The NHANES III study[19] reported a US nationally representative study of body composition, measured by SF-BIA in 1988–94, using prediction equations for FFM and TBW validated against isotope dilution and a multi-compartment model.[20] The subgroup non-Hispanic white 70–80-year olds can be compared to the present study (Table 4). Compared to the US study, our subjects had similar average BMI, lower FFM and thus higher fatness in both genders.

In a non-randomly selected Swiss population with healthy 70–79-year olds, average FFM and fatness was 41 kg and 36% for women and 56 kg and 25% for men[21] (Table 4), calculated with BIA Geneva equations previously validated against DXA. Compared to the Swiss study,[21] our subjects had higher average BW, slightly higher BMI, higher fatness, and quite similar FFM.

A recent Italian study reported nationally representative reference values of body composition measured by DXA in a selected population[22] (Table 4). Compared to our DXA cohort, average BMI for women aged 70–80 years was slightly lower but similar for men. Both Italian genders had lower average fatness and body fat index (BFI) (women 9.6 and men 7.1). Average fat free mass index (FFMI) was similar for women and slightly higher for Italian men.

The differences in body composition in the Swiss, American, Italian and Swedish studies could possibly be explained by different selection of subjects, different reference methods, different BIA/BIS prediction equations or changes in lifestyle. A strength of the present study is that it is based on a population sample and the subjects are representative for their age.

Table 8
BIS prediction equations and DXA. Comparison of TBSMM measured by DXA and calculated from BIS prediction equations in 98 non-institutionalized 75-year-old subjects.

All subjects ($n = 98$)	Mean (SD) (kg)	Min. (kg)	Max. (kg)
$TBSMM_{DxA}$ minus $TBSMM_{50\ kHz}$	0.17 (1.54)	−4.28	4.20
$TBSMM_{DxA}$ minus $TBSMM_{BW}$	−0.10 (1.56)	−4.67	3.62
$TBSMM_{DxA}$ minus $TBSMM_{noBW}$	0.22 (1.61)	−4.70	4.49
Women ($n = 48$)			
$TBSMM_{DxA}$ minus $TBSMM_{50\ kHz}$	0.18 (1.16)	−1.64	2.91
$TBSMM_{DxA}$ minus $TBSMM_{BW}$	−0.10 (1.17)	−2.17	2.60
$TBSMM_{DxA}$ minus $TBSMM_{noBW}$	0.26 (1.24)	−1.95	3.20
Men ($n = 50$)			
$TBSMM_{DxA}$ minus $TBSMM_{50\ kHz}$	0.16 (1.85)	−4.28	4.20
$TBSMM_{DxA}$ minus $TBSMM_{BW}$	−0.09 (1.87)	−4.67	3.62
$TBSMM_{DxA}$ minus $TBSMM_{noBW}$	0.18 (1.90)	−4.70	4.49

Table 9
Comparison of BIS prediction equations. Comparison with paired samples t test of BIS TBSMM prediction equations when applied to 574 non-institutionalized 75-year-old subjects. ns = Non-significant.

	Women ($n = 345$)	p-value	Men ($n = 229$)	p-value
	Mean (kg) (SD)		Mean (kg) (SD)	
$TBSMM_{50\ kHz}$ minus $TBSMM_{BW}$	−0.47 (0.41)	<0.03	-0.32 (0.24)	<0.03
$TBSMM_{50\ kHz}$ minus $TBSMM_{noBW}$	−0.07 (0.67)	ns	0.09 (0.54)	0.04
$TBSMM_{noBW}$ minus $TBSMM_{BW}$	−0,40 (0.46)	<0.03	-0.41 (0.44)	<0.03

4.3. BIS and DXA for assessment of body composition in the elderly

Average FFM_{BIS} was in agreement with FFM_{DxA}, but with a small systematic positive bias, although large individual variation was observed. Average BF_{BIS} was also in agreement with BF_{DxA}, but as expected with a small systematic negative bias, reciprocal to FFM_{BIS} bias.

4.4. Muscle mass prediction

Previously published BIA-equations[4,8] overestimated skeletal muscle mass in our subjects. The overestimations were larger for men than for women for both equations, and particularly for $SMM_{Janssen}$. This could be due to the fact that both muscle mass estimates were developed to include a wide range of ages, perhaps at the cost of less accuracy among the elderly. Average age for the population that generated $SMM_{Janssen}$ was 42 years. Kyle et al. did not report average age, but 48% were >55-year-old.[4] Hence, we found it necessary to develop an age-specific TBSMM BIS prediction equation. Usually, a combination of impedance and anthropometrics are used as predictors in body composition equations.[15] We developed three TBSMM-equations; one using the same independent predictors as Kyle and Janssen[4,8] and two using BIS measurements, i.e. the first one corresponding to SF-BIA. The trunk has limited impact on whole body impedance although it constitutes about 50% of BW.[2] Thus, changes in FFM in the trunk are probably inadequately detected by whole body impedance, although it contributes to BW.[2] Furthermore, healthy subjects, and especially patients may have different proportions between trunk and extremities. Hence, excluding BW as TBSMM predictor might reduce that source of bias.

Comparison of the three developed TBSMM prediction equations resulted in mostly significant but small average differences. Thus, there seems to be neither any advantage nor any disadvantage to predict muscle mass from SF-BIA compared to BIS in our subjects. The two equations that included BIS measurements ($TBSMM_{BW}$ and $TBSMM_{noBW}$) gave slightly different results. However, this difference is of doubtful importance in clinical practise. Thus, the inclusion of BW as an independent predictor of TBSMM will only slightly increase the degree of explanation, and it might lower the accuracy in patients with altered body proportions. SEE for the three developed equations were quite similar. Furthermore, R^2 and R^2_{pred} for all three equations were high and very similar. Hence, we suggest to use the equation $TBSMM_{noBW}$ in future studies.

In conclusion, elderly Swedes have average BMI corresponding to overweight, and also higher than an earlier Swedish cohort. BIS can be used to evaluate average FFM and BF in the elderly, though a small systematic bias was found. Average TBSMM among elderly can be predicted from BIS, although with substantial individual variation.

Conflict of interest

The authors have no conflict of interest.

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The coauthors in this paper have contributed as follows: Marja Tengvall analysed data and wrote the manuscript, Lars Ellegård contributed to analysing data and writing the manuscript, Vibeke Malmros performed the examinations, Niklas Bosaeus made possible the compilation of epidemiological and impedance data, Lauren Lissner was responsible for the Geriatric and Gerontologic Population Studies and the Population Study of Women in Göteborg and contributed to study design and writing of the manuscript, Ingvar Bosaeus initiated and designed the present study and contributed to analysing data and writing the manuscript.

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